INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/17395

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) :Please See Extra Sheet.
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : Please See Extra Sheet.

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,298,429 A (EVANS et al.) 29 March 1994, see entire document.	1-125, 127-129
Y	US 5,514,561 (QUANTE et al.) 07 May 1996, see entire document.	1-125, 127-129
Y	WO 94/24301 (THE UNIVERSITY OF EDINBURGH) 27 October 1994, see entire document.	1-125, 127-129
Y,P	WO 96/30540 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 03 October 1996, see entire document.	1-125, 127-129
X	TADROS et al. Synthesis of quinoline derivatives. Indian Journal of Chemistry. June 1976, Vol 14B, pages 467-469, especially page 468, column 1.	128-131

U. Virol. 1989 3727-3737

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
16 JANUARY 1998	10 FEB 1998
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer JEFFREY FREDMAN Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/17395

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SKARNES et al. A gene trap approach in mouse embryonic stem cells: the lacZ reporter is activated by splicing, reflects endogenous gene expression, and is mutagenic in mice. Genes and Development. 1992, Vol. 6, pages 903-918, see entire document.	1-125, 127-129
Y	REDDY et al. Fluorescence-activated sorting of totipotent embryonic stem cells expressing developmentally regulated lacZ fusion genes. Proc. Natl. Acad. Sci. USA. August 1992, Vol. 89, pages 6721-6725, see entire document.	1-125, 127-129
Y	KUSPA et al. Tagging developmental genes in Dictyostelium by restriction enzyme-mediated integration of plasmid DNA. Proc. Natl. Acad. Sci. USA. 1992, Vol.89, pages 8803-8807, see entire document.	1-125, 127-129
Y	REID et al. Cotransformation and gene targeting in Mouse embryonic stem cells. Molecular and Cellular Biology. May 1991, Vol. 11, No. 5, pages 2769-2777, see entire document.	1-125, 127-129

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PCT/US97/17395

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 126
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/17395

A. CLASSIFICATION OF SUBJECT MATTER:
IPC (6):

C07D 221/02, 215/12; C12Q 1/70, 1/68, 1/08; C12P 21/06; C12N 15/00, 9/14, 9/84, 9/86; G01N 33/53; C07H 21/02, 21/04; A01N 43/04

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

546/112, 174; 435/5, 6, 40.51, 69.1, 69.8, 70.1, 91.1, 172.1, 172.3, 195, 230, 231, 325, 968; 536/23.1, 24.3, 24.31, 24.5; 514/44

B. FIELDS SEARCHED
Minimum documentation searched
Classification System: U.S.

546/112, 174; 435/5, 6, 40.51, 69.1, 69.8, 70.1, 91.1, 172.1, 172.3, 195, 230, 231, 325, 968; 536/23.1, 24.3, 24.31, 24.5; 514/44

B. FIELDS SEARCHED
Electronic data bases consulted (Name of data base and where practicable terms used):

APS, STN REGISTRY, BEILSTEIN ONLINE, BIOSIS, CJACS, DRUGU, EMBASE, EUROPATFULL, MEDLINE, PATOSWO, SCISEARCH, TOXLIT
search terms: lactamase, reporter, marker, label, fluorescen?, gene, trap, ligand, assay, screening, method, vivo, vitro

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1.

Group I, claim(s) 1-125 and 127, drawn to methods for identifying proteins or chemicals/drugs employing beta-lactamase constructs.

Group II, claim(s) 128-131, drawn to chemicals/drugs identified by screening with beta-lactamase constructs.

Note that claim 126 is not listed. It is an improper multiple dependent claim that fails to claim the multiple embodiments in the alternative (PCT Rule 6.4) and is thus withdrawn under nonestablishment. If it were included it would be listed with Group II.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

Applicant is required to elect one species of chemical/drug encompassed by claims 128-131 of Group II selected from modulators of the following:

hormone receptors
intracellular receptors
receptors of the cytokine super family
G-coupled protein receptors
heterologous G-proteins
neurotransmitter receptors
tyrosine kinase receptors
viral components
physiological responses
cellular pathways
chemical A
chemical B

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The inventions listed as Groups I and II do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The chemicals/drugs that are identifiable by the methods of Group I include admittedly old chemicals (description pages 66+). Mere characterization of old chemicals as being active in the assays of Group I cannot impart novelty over the prior art to the chemicals themselves. The claimed invention of Group II thus lacks a special technical feature that defines a contribution over the prior art.

The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: The vast number of chemicals/drugs encompassed by Group II include numerous already known chemicals. These have no common core structure and no common property or activity; further they do not belong to any recognized class of chemical compounds in the art to which the invention pertains.

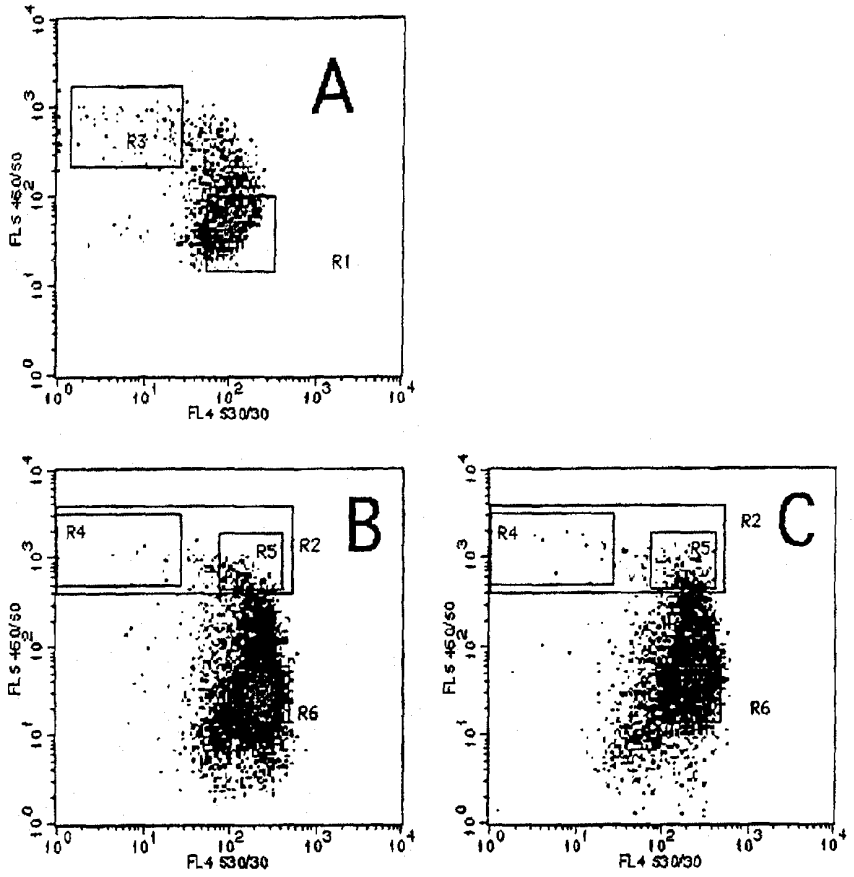

FIG. 4

L Number	Hits	Search Text	DB	Time stamp
1	339	lactamase same (fused or fusion) same cell	USPAT; US-PGPUB	2003/02/14 07:32
2	342	lactamase same (fused or fusion) same cell$4	USPAT; US-PGPUB	2003/02/14 07:33
3	86	lactamase near7 (fused or fusion) same cell$4	USPAT; US-PGPUB	2003/02/14 07:34
4	10	(lactamase near7 (fused or fusion) same cell$4) same promoter	USPAT; US-PGPUB	2003/02/14 07:37
5	2	(lactamase near7 (fused or fusion) same cell$4) same librar$4	USPAT; US-PGPUB	2003/02/14 07:38
6	4	(lactamase same (fused or fusion) same cell$4) same vir$3 near3 vector	USPAT; US-PGPUB	2003/02/14 07:57
7	11	"5928888"	USPAT; US-PGPUB	2003/02/14 07:57
8	0	"5928888" and cell adj1 sensor	USPAT; US-PGPUB	2003/02/14 07:58
9	9	"5928888" and lactamase	USPAT; US-PGPUB	2003/02/14 07:59
10	5	"5928888" and lactamase same fold	USPAT; US-PGPUB	2003/02/14 08:00
11	2	"9717395"	USPAT; US-PGPUB; EPO; DERWENT	2003/02/14 08:01
12	0	SENSITIVE.ti. AND RAPID.ti. and FUNCTIONAL.ti. and IDENTIFICATION.ti and GENOMIC.ti.	USPAT; US-PGPUB; EPO; DERWENT	2003/02/14 08:01
13	0	FUNCTIONAL.ti. and IDENTIFICATION.ti and GENOMIC.ti.	USPAT; US-PGPUB; EPO; DERWENT	2003/02/14 08:01
14	31	FUNCTIONAL.ti. and GENOMIC.ti.	USPAT; US-PGPUB; EPO; DERWENT	2003/02/14 08:02
15	1406	whitney$.in.	USPAT; US-PGPUB; EPO; DERWENT	2003/02/14 08:02
16	5	whitney$.in. and lactamase	USPAT; US-PGPUB; EPO; DERWENT	2003/02/14 08:08
17	155	promoter near2 trap$4	USPAT; US-PGPUB; EPO; DERWENT	2003/02/14 08:08
18	9	"5928888" and lactamase	USPAT; US-PGPUB; EPO; DERWENT	2003/02/14 08:10
19	27	(promoter near2 trap$4) and lactamase	USPAT; US-PGPUB; EPO; DERWENT	2003/02/14 08:10

```
=> d his

     (FILE 'HOME' ENTERED AT 07:55:51 ON 14 FEB 2003)

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 07:56:12 ON 14 FEB 2003
L1             3 S LACTAMASE (9A) FUS? (9A) LIBRAR?
L2         37592 S (VIRUS OR VIRAL) (7A) VECTOR#
L3         33428 S LACTAMASE#
L4             3 S L2 (9A) L3
L5            59 S L2 AND L3
L6            57 DUP REM L5 (2 DUPLICATES REMOVED)
L7           221 S PROMOTER (W) TRAP
L8             0 S L7 AND L3
L9           329 S PROMOTER (W) TRAP?
L10            0 S L9 AND L3
L11         1264 S LACTAMASE# AND PROMOTER#
L12            1 S LACTAMASE# AND PROMOTER# (3A) TRAP?
L13          535 S PROMOTER (9A) TRAP?
L14            3 S L13 AND LACTAMASE

     FILE 'STNGUIDE' ENTERED AT 08:14:19 ON 14 FEB 2003

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 08:15:34 ON 14 FEB 2003
L15         1488 S GENE (3A) TRAP?
L16            7 S L15 AND LACTAMASE#
L17            4 DUP REM L16 (3 DUPLICATES REMOVED)
L18        29560 S LACTAMASE
L19           60 S BLEC
L20           48 S BLAC
L21        26077 S LAC

=> s l15 or l9
L22         1751 L15 OR L9

=> s l22 and (lac or lactam?)
L23           50 L22 AND (LAC OR LACTAM?)

=> dup rem l23
PROCESSING COMPLETED FOR L23
L24           44 DUP REM L23 (6 DUPLICATES REMOVED)

=> d 1-44 ti

L24  ANSWER 1 OF 44      MEDLINE                              DUPLICATE 1
TI   Design of an HIV-1 lentiviral-based gene-trap vector
     to detect developmentally regulated genes in mammalian cells.

L24  ANSWER 2 OF 44      MEDLINE
TI   Visualization of whole-mount skeletal expression patterns of LacZ
     reporters using a tissue clearing protocol.

L24  ANSWER 3 OF 44      MEDLINE
TI   Identification of radiation-responsive genes in vitro using a gene
     trap strategy predicts for modulation of expression by radiation
     in vivo.

L24  ANSWER 4 OF 44  CAPLUS  COPYRIGHT 2003 ACS
TI   Interaction trap assays using selectable markers to screen large libraries
     for protein-protein and protein-nucleic acid interactions
```

L24 ANSWER 5 OF 44 CAPLUS COPYRIGHT 2003 ACS
TI Signal sequence **trapping** from existing **gene** library using a transposon containing a promoter-less and signal-less secretion reporter

L24 ANSWER 6 OF 44 MEDLINE
TI Craniofacial dysmorphogenesis including cleft palate in mice with an insertional mutation in the discs large gene.

L24 ANSWER 7 OF 44 MEDLINE
TI **Gene-trap** mutagenesis: past, present and beyond.

L24 ANSWER 8 OF 44 MEDLINE
TI The ROSA26 LacZ-neo(R) insertion confers resistance to mammary tumors in Apc(Min/+) mice.

L24 ANSWER 9 OF 44 MEDLINE
TI Sorting nexin-14, a **gene** expressed in motoneurons **trapped** by an in vitro preselection method.

L24 ANSWER 10 OF 44 MEDLINE
TI Developmental regulation and complex organization of the promoter of the non-coding hsr(omega) gene of Drosophila melanogaster.

L24 ANSWER 11 OF 44 MEDLINE
TI Isolation of a novel insertion sequence from Mycobacterium fortuitum using a trap vector based on inactivation of a lacZ reporter gene.

L24 ANSWER 12 OF 44 CAPLUS COPYRIGHT 2003 ACS
TI Interaction trap assay and its reagents

L24 ANSWER 13 OF 44 MEDLINE
TI A retroviral **gene trap** insertion into the histone 3.3A gene causes partial neonatal lethality, stunted growth, neuromuscular deficits and male sub-fertility in transgenic mice.

L24 ANSWER 14 OF 44 MEDLINE
TI Expression of a truncated receptor protein tyrosine phosphatase kappa in the brain of an adult transgenic mouse.

L24 ANSWER 15 OF 44 MEDLINE DUPLICATE 2
TI Developing targets for drug discovery using genome-wide **gene trapping** and ultra-sensitive beta-**lactamase** reporters.

L24 ANSWER 16 OF 44 CAPLUS COPYRIGHT 2003 ACS
TI An interaction trap assay system using the .lambda. repressor for use in a bacterial host

L24 ANSWER 17 OF 44 MEDLINE DUPLICATE 3
TI Expression trapping: identification of novel genes expressed in hematopoietic and endothelial lineages by **gene trapping** in ES cells.

L24 ANSWER 18 OF 44 MEDLINE
TI Selective disruption of genes transiently induced in differentiating mouse embryonic stem cells by using **gene trap** mutagenesis and site-specific recombination.

L24 ANSWER 19 OF 44 MEDLINE
TI Sequence and expression of a novel mouse gene PRDC (protein related to DAN and cerberus) identified by a **gene trap** approach.

L24 ANSWER 20 OF 44 MEDLINE
TI Disruption of murine alpha-enolase by a retroviral **gene trap** results in early embryonic lethality.

L24 ANSWER 21 OF 44 MEDLINE
TI **Gene trap** integrations expressed in the developing heart: insertion site affects splicing of the PT1-ATG vector.

L24 ANSWER 22 OF 44 MEDLINE
TI Compensation for a **gene trap** mutation in the murine microtubule-associated protein 4 locus by alternative polyadenylation and alternative splicing.

L24 ANSWER 23 OF 44 MEDLINE
TI Dmd(mdx-beta geo): a new allele for the mouse dystrophin gene.

L24 ANSWER 24 OF 44 MEDLINE
TI The mouse Gtl2 gene is differentially expressed during embryonic development, encodes multiple alternatively spliced transcripts, and may act as an RNA.

L24 ANSWER 25 OF 44 MEDLINE
TI **Gene trap** expression and mutational analysis for genes involved in the development of the mammalian nervous system.

L24 ANSWER 26 OF 44 MEDLINE
TI Efficient **gene trap** screening for novel developmental genes using IRES beta geo vector and in vitro preselection.

L24 ANSWER 27 OF 44 MEDLINE
TI Restricted beta-galactosidase expression of a hygromycin-lacZ gene targeted to the beta-actin locus and embryonic lethality of beta-actin mutant mice.

L24 ANSWER 28 OF 44 MEDLINE
TI A **gene trap** approach to isolate mammalian genes involved in the cellular response to genotoxic stress.

L24 ANSWER 29 OF 44 MEDLINE
TI An alpha-E-catenin **gene trap** mutation defines its function in preimplantation development.

L24 ANSWER 30 OF 44 MEDLINE
TI A molecular strategy designed for the rapid screening of **gene traps** based on sequence identity and gene expression pattern in adult mice.

L24 ANSWER 31 OF 44 MEDLINE
TI Trapping genes expressed in the developing mouse inner ear.

L24 ANSWER 32 OF 44 MEDLINE
TI Use of a **promoter-trap** retrovirus to identify and isolate genes involved in differentiation of a myeloid progenitor cell line in vitro.

L24 ANSWER 33 OF 44 MEDLINE
TI Sequence and expression pattern of an evolutionarily conserved transcript identified by **gene trapping**.

L24 ANSWER 34 OF 44 MEDLINE
TI A **gene trap** strategy for identifying the gene expressed in the embryonic nervous system.

L24 ANSWER 35 OF 44 MEDLINE
TI Unexpected behavior of a **gene trap** vector comprising a fusion between the Sh ble and the lacZ genes.

L24 ANSWER 36 OF 44 MEDLINE
TI Gtl2lacZ, an insertional mutation on mouse chromosome 12 with parental origin-dependent phenotype.

L24 ANSWER 37 OF 44 MEDLINE
TI An enhanced **promoter trap** protocol.

L24 ANSWER 38 OF 44 MEDLINE
TI Characterization of a **gene trap** insertion into a novel gene, cordon-bleu, expressed in axial structures of the gastrulating mouse embryo.

L24 ANSWER 39 OF 44 MEDLINE DUPLICATE 4
TI Directed overexpression of suppressor 2 of zeste and Posterior Sex Combs results in bristle abnormalities in Drosophila melanogaster.

L24 ANSWER 40 OF 44 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI **Gene** and enhancer **trap** screens in ES cell chimeras.

L24 ANSWER 41 OF 44 MEDLINE
TI A **gene trap** approach in mouse embryonic stem cells: the lacZ reported is activated by splicing, reflects endogenous gene expression, and is mutagenic in mice.

L24 ANSWER 42 OF 44 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI RETROVIRUS **PROMOTER-TRAP** VECTOR TO INDUCE **LAC** -Z GENE FUSIONS IN MAMMALIAN CELLS.

L24 ANSWER 43 OF 44 MEDLINE
TI '**Promoter trapping**' in Caenorhabditis elegans.

L24 ANSWER 44 OF 44 CAPLUS COPYRIGHT 2003 ACS
TI Analysis of transfer genes and gene products within the traB-traC region of the Escherichia coli fertility factor, F

=> d 37 bib ab

L24 ANSWER 37 OF 44 MEDLINE
AN 95375434 MEDLINE
DN 95375434 PubMed ID: 7647466
TI An enhanced **promoter trap** protocol.
AU Toyoda A; Kusuda J; Maeda H; Hashimoto K
CS Division of Genetic Resources, National Institute of Health, Tokyo, Japan.
SO MAMMALIAN GENOME, (1995 Jun) 6 (6) 426-8.
Journal code: 9100916. ISSN: 0938-8990.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199509
ED Entered STN: 19951005
Last Updated on STN: 19970203
Entered Medline: 19950926

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	27.09	114.37

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.30	-8.46

FILE 'STNGUIDE' ENTERED AT 08:20:49 ON 14 FEB 2003

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 7, 2003 (20030207/UP).

=> d 35 bib ab
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, BIOSIS, CAPLUS' - CONTINUE? (Y)/N:y

L24 ANSWER 35 OF 44 MEDLINE
AN 97073311 MEDLINE
DN 97073311 PubMed ID: 8916035
TI Unexpected behavior of a **gene trap** vector comprising a fusion between the Sh ble and the lacZ genes.
AU Camus A; Kress C; Babinet C; Barra J
CS Departement d'Immunologie, URA CNRS 1960, Institut Pasteur, Paris, France.
SO MOLECULAR REPRODUCTION AND DEVELOPMENT, (1996 Nov) 45 (3) 255-63.
Journal code: 8903333. ISSN: 1040-452X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
ED Entered STN: 19970523
Last Updated on STN: 19970523
Entered Medline: 19970513
AB A new **gene trap** vector has been designed, comprised of a fusion between the Sh ble gene, which confers resistance to the antibiotic phleomycin, and the lacZ gene (phleal fusion gene). A synthetic splice acceptor, made of the yeast branchpoint followed by a pyrimidin-rich sequence of 27 nucleotides, is included at the 5' extremity. The linearized **gene trap** vector was introduced into mouse embryonic stem cells (ES cells), and 40 phleomycin resistant (phleo') cell lines possessing a single copy of the insert were selected. They were stable in expressing the lacZ gene. Reporter gene expression was studied at days 8.5 and 10.5 of embryonic development in chimeric embryos obtained after injection of phleo' ES clones into 8-cell stage embryos. Out of 20 phleal lines examined, 14 exhibited beta-galactosidase expression at day 10.5. Use of the phleal fusion **gene trap** vector to select genes expressed in ES cells, therefore, is compatible with the isolation of genes expressed at midgestation. However, and most intriguingly, 10 out of these 14 cell lines (71%) displayed reporter gene expression mostly in heart and liver. Two of them exhibited, in addition, expression in central nervous system (CNS) or in CNS and limb buds, respectively. Germline chimeras were subsequently obtained and 15 mouse lines have been established. Intercrosses of animals heterozygous for the insertion revealed a mutant phenotype in several lines.

=> d 28-33 bib ab
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, BIOSIS, CAPLUS' - CONTINUE? (Y)/N:y

L24 ANSWER 28 OF 44 MEDLINE
AN 1998033391 MEDLINE
DN 98033391 PubMed ID: 9365260
TI A **gene trap** approach to isolate mammalian genes involved in the cellular response to genotoxic stress.
AU Menichini P; Viaggi S; Gallerani E; Fronza G; Ottaggio L; Comes A; Ellwart J W; Abbondandolo A
CS CSTA-Laboratory of Mutagenesis, National Institute for Research on Cancer (IST), Largo Rosanna Benzi, 10, Genoa, Italy.. menikini@hp380.ist.unige.it
SO NUCLEIC ACIDS RESEARCH, (1997 Dec 1) 25 (23) 4803-7.
Journal code: 0411011. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-Y11338
EM 199801
ED Entered STN: 19980130
Last Updated on STN: 19980130
Entered Medline: 19980120
AB Treatment of cells with DNA damaging agents leads to induction of a variety of genes involved in different cellular processes. We have applied a lacZ-based **gene trap** strategy to search for new mammalian genes induced by genotoxic stress. A population of 32 x 10(3) neo r clones stably transfected with a **gene trap** vector was obtained, stained with fluorescein di-beta-d-galactopyranoside and analyzed by flow activated cell sorting and replica plating. This strategy allowed isolation of 30 neo r 'putative inducible' cell lines expressing lacZ only after a DNA damaging treatment. For three clones the site of integration and the degree of inducibility after UV treatment were determined by Southern blot and beta-galactosidase measurement respectively. One cell line (clone VI) showed a single integration site and a reproducible 3-fold induction of beta-galactosidase activity following UV irradiation. Fused transcripts were isolated from induced cells and a portion of the **trapped gene** was amplified by rapid amplification of cDNA ends. Sequence analysis and comparison with available gene and protein databanks revealed that the gene was novel.

L24 ANSWER 29 OF 44 MEDLINE
AN 97175699 MEDLINE
DN 97175699 PubMed ID: 9023354
TI An alpha-E-catenin **gene trap** mutation defines its function in preimplantation development.
AU Torres M; Stoykova A; Huber O; Chowdhury K; Bonaldo P; Mansouri A; Butz S; Kemler R; Gruss P
CS Abteilung Molekulare Zellbiologie, Max-Planck-Institut fur Biophysikalische Chemie, Gottingen, Germany.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1997 Feb 4) 94 (3) 901-6.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199703
ED Entered STN: 19970321
Last Updated on STN: 19970321

Entered Medline: 19970310

AB Catenins are proteins associated with the cytoplasmic domain of cadherins, a family of transmembrane cell adhesion molecules. The cadherin-catenin adhesion system is involved in morphogenesis during development and in the maintenance of the integrity of different tissue types. Using a **gene trap** strategy, we have isolated a mouse mutation for the gene encoding the alpha-E-catenin. This form of the alpha-catenin appears frequently coexpressed with E-cadherin in epithelial cell types. The mutation obtained eliminates the carboxyl-terminal third of the protein but nevertheless provokes a complete loss-of-function phenotype. Homozygous mutants show disruption of the trophoblast epithelium (the first differentiated embryonic tissue), and development is consequently blocked at the blastocyst stage. This phenotype parallels the defects observed in E-cadherin mutant embryos. Our results show the requirement of the alpha-E-catenin carboxy terminus for its function and represent evidence of the role of the alpha-E-catenin in vivo, identifying this molecule as the natural partner of the E-cadherin in trophoblast epithelium.

L24 ANSWER 30 OF 44 MEDLINE
AN 97185248 MEDLINE
DN 97185248 PubMed ID: 9032982
TI A molecular strategy designed for the rapid screening of **gene traps** based on sequence identity and gene expression pattern in adult mice.
AU Holzschu D; Lapierre L; Neubaum D; Mark W H
CS Section of Genetics & Development, Cornell University, Ithaca, NY 14853, USA.
NC 5 T32 GM07617 (NIGMS)
SO TRANSGENIC RESEARCH, (1997 Jan) 6 (1) 97-106.
Journal code: 9209120. ISSN: 0962-8819.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X98134; GENBANK-X98198; GENBANK-X98199; GENBANK-X98200; GENBANK-X98201; GENBANK-X98202; GENBANK-X98203; GENBANK-X98204
EM 199703
ED Entered STN: 19970327
Last Updated on STN: 19990129
Entered Medline: 19970317
AB We have devised a strategy to rapidly screen **gene traps** in mouse embryonic stem (ES) cells based on DNA sequence information and an in vitro analysis of gene expression. After the initial identification of ES cell clones expressing beta-galactosidase, tagged RNA transcripts were immediately cloned and sequenced in order to determine their identities. Novel gene sequences found were used to probe northern blots to examine the expression patterns of their cognate genes. Our initial characterization of 30 cDNA clones indicated that more than half of the tagged sequences were novel mouse genes and of these 40% showed a restricted pattern of expression in adult mouse tissues. This molecular characterization of **gene traps** is quick, reliable and well suited for the large-scale screening of mammalian developmental genes. Furthermore, since **gene trap** insertion frequently disrupts the tagged host gene, the ES cells can be used to produce transgenic animals for a genetic analysis of gene function.

L24 ANSWER 31 OF 44 MEDLINE
AN 1998107607 MEDLINE
DN 98107607 PubMed ID: 9447918
TI Trapping genes expressed in the developing mouse inner ear.
AU Yang W; Musci T S; Mansour S L

CS Department of Human Genetics, Eccles Institute of Human Genetics, University of Utah, Salt Lake City 84112, USA.
NC DC02043 (NIDCD)
SO HEARING RESEARCH, (1997 Dec) 114 (1-2) 53-61.
Journal code: 7900445. ISSN: 0378-5955.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199803
ED Entered STN: 19980312
Last Updated on STN: 19980312
Entered Medline: 19980303
AB Identification of the genes involved in the development of the mouse inner ear and developmental studies of mice that bear mutations in these genes is an important approach to understanding genetically determined human auditory dysfunction. Towards this end, we initiated a **gene trap** screen designed to simultaneously mark and mutate genes in mouse embryonic stem cells by the insertion of a lacZ reporter gene. Expression of beta-galactosidase in **gene trap** cell lines was monitored both before and after the addition of factors that are known to affect inner ear development. **Gene trap** cell lines that expressed beta-galactosidase under one or more culture conditions were used to create chimeric mouse embryos for studies of reporter gene expression in vivo. A high proportion of these **gene trap** insertions were expressed in the developing inner ear, suggesting that this strategy provides an effective means of identifying genes that may be involved in inner ear development or function.

L24 ANSWER 32 OF 44 MEDLINE
AN 96202499 MEDLINE
DN 96202499 PubMed ID: 8634423
TI Use of a **promoter-trap** retrovirus to identify and isolate genes involved in differentiation of a myeloid progenitor cell line in vitro.
AU Jonsson J I; Wu Q; Nilsson K; Phillips R A
CS Division of Immunology and Cancer Research, Hospital for Sick Children, Toronto, Ontario, Canada.
SO BLOOD, (1996 Mar 1) 87 (5) 1771-9.
Journal code: 7603509. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
OS GENBANK-J02836; GENBANK-J03267; GENBANK-M23458; GENBANK-M86440; GENBANK-M92096; GENBANK-S23500; GENBANK-U12259
EM 199607
ED Entered STN: 19960719
Last Updated on STN: 19970203
Entered Medline: 19960710
AB Studies of gene regulation during early hematopoiesis and of the regulatory network that controls differentiation and lineage commitment are hampered by difficulties in isolating and growing stem cells and early progenitor cells. These difficulties preclude the application of standard molecular genetic approaches to these problems. As an alternative approach we have introduced a lacZ-containing **promoter-trap** retrovirus into hematopoietic cells. We used the interleukin-3-dependent mouse myeloid progenitor cell 32D as a model to identify transcriptionally active genes. The frequency of integrations that led to transcription of the lacZ gene was estimated to be 0.5% of all integrations, of which 14% were downregulated on differentiation of 32D cells towards neutrophils. Thus, one in every 1,000 to 2,000 integrations identified a

developmentally regulated gene. Cellular DNA sequences upstream of proviral integrations were isolated by inverse polymerase chain reaction. Five were further characterized and we confirmed by RNA expression analysis that they were downregulated on differentiation. Sequence analysis revealed identification of novel genes with sequence similarity to known genes. Considering the high efficiency of retroviral infection, our study shows the feasibility of using **promoter-trap** vectors to identity and isolate developmentally regulated genes from early hematopoietic progenitors.

L24 ANSWER 33 OF 44 MEDLINE
AN 96305352 MEDLINE
DN 96305352 PubMed ID: 8688464
TI Sequence and expression pattern of an evolutionarily conserved transcript identified by **gene trapping**.
AU Rijkers T; Ruther U
CS Medizinische Hochschule Hannover, Institut fur Molekularbiologie, Germany.
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1996 Jul 17) 1307 (3) 294-300.
Journal code: 0217513. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-Z54179
EM 199608
ED Entered STN: 19960911
Last Updated on STN: 19960911
Entered Medline: 19960829
AB We have isolated and analysed embryonic stem (ES) cell clones after electroporation with a **gene trap** vector. Clones were screened for changes in their lacZ reporter gene activity upon in vitro differentiation. The cDNA of one of the trapped transcripts, T10-2A2, was isolated and analysed in detail. Although not expressed constitutively in differentiating ES cells, the transcript was present in most organs of adult mice and widely expressed in midgestation mouse embryos. Zoo blot analysis indicated a conservation of this novel gene in yeast, rat and human.

=> d 7 bib ab
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, BIOSIS, CAPLUS' - CONTINUE? (Y)/N:y

L24 ANSWER 7 OF 44 MEDLINE
AN 2001536715 MEDLINE
DN 21468432 PubMed ID: 11584292
TI **Gene-trap** mutagenesis: past, present and beyond.
AU Stanford W L; Cohn J B; Cordes S P
CS Programme in Development and Fetal Health, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, 600 University Avenue, Room 983, Toronto, Ontario, Canada M5G 1X5.. stanford@mshri.on.ca
SO Nat Rev Genet, (2001 Oct) 2 (10) 756-68. Ref: 103
Journal code: 100962779. ISSN: 1471-0056.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 20011004

Last Updated on STN: 20020122
Entered Medline: 20011205

AB Although at least 35,000 human genes have been sequenced and mapped, adequate expression or functional information is available for only approximately 15% of them. **Gene-trap** mutagenesis is a technique that randomly generates loss-of-function mutations and reports the expression of many mouse genes. At present, several large-scale, **gene-trap** screens are being carried out with various new vectors, which aim to generate a public resource of mutagenized embryonic stem (ES) cells. This resource now includes more than 8,000 mutagenized ES-cell lines, which are freely available, making it an appropriate time to evaluate the recent advances in this area of genomic technology and the technical hurdles it has yet to overcome.

=> d his

(FILE 'HOME' ENTERED AT 07:55:51 ON 14 FEB 2003)

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 07:56:12 ON 14 FEB 2003

L1	3	S	LACTAMASE (9A) FUS? (9A) LIBRAR?
L2	37592	S	(VIRUS OR VIRAL) (7A) VECTOR#
L3	33428	S	LACTAMASE#
L4	3	S	L2 (9A) L3
L5	59	S	L2 AND L3
L6	57	DUP REM	L5 (2 DUPLICATES REMOVED)
L7	221	S	PROMOTER (W) TRAP
L8	0	S	L7 AND L3
L9	329	S	PROMOTER (W) TRAP?
L10	0	S	L9 AND L3
L11	1264	S	LACTAMASE# AND PROMOTER#
L12	1	S	LACTAMASE# AND PROMOTER# (3A) TRAP?
L13	535	S	PROMOTER (9A) TRAP?
L14	3	S	L13 AND LACTAMASE

FILE 'STNGUIDE' ENTERED AT 08:14:19 ON 14 FEB 2003

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 08:15:34 ON 14 FEB 2003

L15	1488	S	GENE (3A) TRAP?
L16	7	S	L15 AND LACTAMASE#
L17	4	DUP REM	L16 (3 DUPLICATES REMOVED)
L18	29560	S	LACTAMASE
L19	60	S	BLEC
L20	48	S	BLAC
L21	26077	S	LAC
L22	1751	S	L15 OR L9
L23	50	S	L22 AND (LAC OR LACTAM?)
L24	44	DUP REM	L23 (6 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 08:20:49 ON 14 FEB 2003

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 08:21:16 ON 14 FEB 2003

FILE 'STNGUIDE' ENTERED AT 08:21:16 ON 14 FEB 2003

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 08:22:09 ON 14 FEB 2003

FILE 'STNGUIDE' ENTERED AT 08:22:09 ON 14 FEB 2003

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 08:23:18 ON 14 FEB 2003

FILE 'STNGUIDE' ENTERED AT 08:23:18 ON 14 FEB 2003

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=> file medline biosis caplus
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     (FILE 'HOME' ENTERED AT 07:55:51 ON 14 FEB 2003)

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 07:56:12 ON 14 FEB 2003
L1             3 S LACTAMASE (9A) FUS? (9A) LIBRAR?
L2         37592 S (VIRUS OR VIRAL) (7A) VECTOR#
L3         33428 S LACTAMASE#
L4             3 S L2 (9A) L3
L5            59 S L2 AND L3
L6            57 DUP REM L5 (2 DUPLICATES REMOVED)
L7           221 S PROMOTER (W) TRAP
L8             0 S L7 AND L3
L9           329 S PROMOTER (W) TRAP?
L10            0 S L9 AND L3
L11         1264 S LACTAMASE# AND PROMOTER#
L12            1 S LACTAMASE# AND PROMOTER# (3A) TRAP?
L13          535 S PROMOTER (9A) TRAP?
L14            3 S L13 AND LACTAMASE

     FILE 'STNGUIDE' ENTERED AT 08:14:19 ON 14 FEB 2003

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 08:15:34 ON 14 FEB 2003
L15         1488 S GENE (3A) TRAP?
L16            7 S L15 AND LACTAMASE#
L17            4 DUP REM L16 (3 DUPLICATES REMOVED)
L18        29560 S LACTAMASE
L19           60 S BLEC
L20           48 S BLAC
L21        26077 S LAC
L22         1751 S L15 OR L9
L23           50 S L22 AND (LAC OR LACTAM?)
L24           44 DUP REM L23 (6 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 08:20:49 ON 14 FEB 2003

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 08:21:16 ON 14 FEB 2003

     FILE 'STNGUIDE' ENTERED AT 08:21:16 ON 14 FEB 2003

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 08:22:09 ON 14 FEB 2003
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FILE 'STNGUIDE' ENTERED AT 08:22:09 ON 14 FEB 2003

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 08:23:18 ON 14 FEB 2003

FILE 'STNGUIDE' ENTERED AT 08:23:18 ON 14 FEB 2003

FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 08:23:46 ON 14 FEB 2003

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=> s fus? (9a) lactamase#
L25          784 FUS? (9A) LACTAMASE#

=> s l25 and py<1998
   2 FILES SEARCHED...
L26          608 L25 AND PY<1998

=> s l26 and (promoter# or trap?)
L27          113 L26 AND (PROMOTER# OR TRAP?)

=> dup rem l27
PROCESSING COMPLETED FOR L27
L28           59 DUP REM L27 (54 DUPLICATES REMOVED)

=> d 1-59 ti

L28  ANSWER 1 OF 59  CAPLUS  COPYRIGHT 2003 ACS
TI   DNA and protein sequences of murine and human neurotactin chemokine and
     its therapeutic applications

L28  ANSWER 2 OF 59  CAPLUS  COPYRIGHT 2003 ACS
TI   Inhibitors of global pathogenesis gene regulators for treatment of
     microbial infections, pharmaceutical compositions, and screening methods

L28  ANSWER 3 OF 59      MEDLINE                              DUPLICATE 1
TI   A novel gene, algK, from the alginate biosynthesis cluster of Pseudomonas
     aeruginosa.

L28  ANSWER 4 OF 59  CAPLUS  COPYRIGHT 2003 ACS
TI   Preliminary characterization of a TolA-.beta.-lactamase hybrid protein for
     polypeptide display at the surface of liposomes.

L28  ANSWER 5 OF 59      MEDLINE                              DUPLICATE 2
TI   Inhibition of Serratia marcescens nuclease secretion by a truncated
     nuclease peptide.

L28  ANSWER 6 OF 59  CAPLUS  COPYRIGHT 2003 ACS
TI   Recombinant BCG expressing the Leishmania surface antigen Gp63 induces
     protective immunity against Leishmania major infection in BALB/c mice

L28  ANSWER 7 OF 59      MEDLINE                              DUPLICATE 3
TI   Secretion of active beta-lactamase to the medium mediated by the
     Escherichia coli haemolysin transport pathway.

L28  ANSWER 8 OF 59  CAPLUS  COPYRIGHT 2003 ACS
TI   Cloning of .alpha.-1,3-glucanase from Bacillus circulans and dextranase
     from Arthrobacter for use as dentifrices

L28  ANSWER 9 OF 59      MEDLINE                              DUPLICATE 4
TI   Use of beta-lactamase as a secreted reporter of promoter
     function in yeast.

L28  ANSWER 10 OF 59      MEDLINE                             DUPLICATE 5
TI   Transcription and expression analysis, using lacZ and phoA gene
```

fusions, of Mycobacterium fortuitum beta-**lactamase** genes cloned from a natural isolate and a high-level beta-lactamase producer.

L28 ANSWER 11 OF 59 MEDLINE DUPLICATE 6
TI Expression of Caulobacter dnaA as a function of the cell cycle.

L28 ANSWER 12 OF 59 MEDLINE DUPLICATE 7
TI Use of the tetracycline **promoter** for the tightly regulated production of a murine antibody fragment in Escherichia coli.

L28 ANSWER 13 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Universal .beta.-galactosidase cloning vectors for **promoter** analysis and gene targeting

L28 ANSWER 14 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Manufacture of streptavidin by expression of the sav gene in Bacillus subtilis

L28 ANSWER 15 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Live dysentery vaccines using fusion proteins containing fragments of shigatoxin and the Escherichia coli lamB gene product

L28 ANSWER 16 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI A fusion protein of Shiga toxin subunit B and hemolysin A and its secretory manufacture in Salmonella typhimurium

L28 ANSWER 17 OF 59 MEDLINE DUPLICATE 8
TI Genetic construction, expression, and characterization of a single chain anti-carcinoma antibody **fused** to beta-**lactamase**.

L28 ANSWER 18 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Gene technological studies of an alpha-amylase based expression system in 'Streptomyces'. 1. Construction of a regulated secretion vector for heterologous expression in 'Streptomyces lividans'

L28 ANSWER 19 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Antigen-enzyme conjugate expression and detection system

L28 ANSWER 20 OF 59 MEDLINE DUPLICATE 9
TI Disulphide bridge formation in the periplasm of Escherichia coli: beta-**lactamase**:: human IgG3 hinge **fusions** as a model system.

L28 ANSWER 21 OF 59 MEDLINE DUPLICATE 10
TI Overproduction of biologically-active human nerve growth factor in Escherichia coli.

L28 ANSWER 22 OF 59 MEDLINE DUPLICATE 11
TI Extracellular export of Shiga toxin B-subunit/haemolysin A (C-terminus) fusion protein expressed in Salmonella typhimurium aroA-mutant and stimulation of B-subunit specific antibody responses in mice.

L28 ANSWER 23 OF 59 MEDLINE
TI Targeting sequences of the two major peroxisomal proteins in the methylotrophic yeast Hansenula polymorpha.

L28 ANSWER 24 OF 59 MEDLINE DUPLICATE 12
TI Efficient secretion in yeast based on fragments from K1 killer preprotoxin.

L28 ANSWER 25 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Secretion of Escherichia coli .beta.-lactamase from Bacillus subtilis with the aid of usefully constructed secretion vector

L28 ANSWER 26 OF 59 MEDLINE DUPLICATE 13
TI Regulation of the protein A-encoding gene in Staphylococcus aureus.

L28 ANSWER 27 OF 59 MEDLINE DUPLICATE 14
TI Use of a triple protease-deficient mutant of Bacillus subtilis as a host for secretion of a B. subtilis cellulase and TEM beta-lactamase.

L28 ANSWER 28 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Secretion of Bacillus subtilis cytidine deaminase by the aid of signal sequences in Escherichia coli

L28 ANSWER 29 OF 59 MEDLINE DUPLICATE 15
TI Production and secretion in Escherichia coli of hepatitis B virus pre-S2 antigen as **fusion** proteins with beta-**lactamase**.

L28 ANSWER 30 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Amplified expression vector for recombinant manufacture of hepatitis B (HBV) virus

L28 ANSWER 31 OF 59 MEDLINE
TI Staphylococcus aureus chromosomal mutation plaC1 amplifies plasmid pT181 by depressing synthesis of its negative-effector countertranscripts.

L28 ANSWER 32 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Construction of synthetic DNA and its use in large polypeptide synthesis

L28 ANSWER 33 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Transforming growth factor type .alpha. of human and its gene expression from a synthetic DNA

L28 ANSWER 34 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Epidermal growth factor (EGF) of rats and its recombinant manufacture

L28 ANSWER 35 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Gene fusion vectors in Staphylococcus carnosus

L28 ANSWER 36 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI A system for the inducible secretion of proteins from Bacillus subtilis during logarithmic growth

L28 ANSWER 37 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Highly efficient expression of .beta.-lactamase gene in Escherichia coli

L28 ANSWER 38 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI .beta.-Urogastrone secretion by Escherichia

L28 ANSWER 39 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Secretion and expression plasmid vectors containing .beta.-urogastrone gene

L28 ANSWER 40 OF 59 MEDLINE DUPLICATE 16
TI Primary structure of an aminoglycoside 6'-N-acetyltransferase AAC(6')-4, fused in vivo with the signal peptide of the Tn3-encoded beta-lactamase.

L28 ANSWER 41 OF 59 MEDLINE DUPLICATE 17
TI Measurement of cat expression from growth-rate-regulated **promoters** employing beta-lactamase activity as an indicator of plasmid copy number.

L28 ANSWER 42 OF 59 MEDLINE DUPLICATE 18
TI Modulation of Bacillus subtilis alpha-amylase **promoter** activity by the presence of a palindromic sequence in front of the gene.

L28 ANSWER 43 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Protein production and the vector, recombinant DNA and transformant used for this process

L28 ANSWER 44 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Molecular cloning of a .beta.-urogastrone gene and the manufacture of .beta.-urogastrone

L28 ANSWER 45 OF 59 MEDLINE DUPLICATE 19
TI Transfer of fatty acids from the 1-position of phosphatidylethanolamine to the major outer membrane lipoprotein of Escherichia coli.

L28 ANSWER 46 OF 59 MEDLINE DUPLICATE 20
TI Analysis of the primary structure and **promoter** function of a pyruvate decarboxylase gene (PDC1) from Saccharomyces cerevisiae.

L28 ANSWER 47 OF 59 MEDLINE DUPLICATE 21
TI Secretion activities of Bacillus subtilis alpha-amylase signal peptides of different lengths in Escherichia coli cells.

L28 ANSWER 48 OF 59 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 22
TI PROTEOLYTIC PROCESSING OF GLUCOAMYLASE IN THE YEAST SACCHAROMYCES-DIASTATICUS.

L28 ANSWER 49 OF 59 MEDLINE DUPLICATE 23
TI The overproduction and characterization of the bacteriophage Mu regulatory DNA-binding protein ner.

L28 ANSWER 50 OF 59 MEDLINE DUPLICATE 24
TI Expression of a wheat alpha-amylase gene in Escherichia coli: recognition of the translational initiation site and the signal peptide.

L28 ANSWER 51 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Fusions of secreted proteins to alkaline phosphatase: An approach for studying protein secretion

L28 ANSWER 52 OF 59 MEDLINE DUPLICATE 25
TI Translational coupling at the intercistronic boundary of an artificially constructed operon in Escherichia coli.

L28 ANSWER 53 OF 59 MEDLINE DUPLICATE 26
TI Length and structural effect of signal peptides derived from Bacillus subtilis alpha-amylase on secretion of Escherichia coli beta-lactamase in B. subtilis cells.

L28 ANSWER 54 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Secretion vector of Bacillus subtilis constructed from the Bacillus subtilis .alpha.-amylase **promoter** and signal peptide coding region

L28 ANSWER 55 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI Expression of a .beta.-**lactamase** preproinsulin **fusion** protein in Escherichia coli

L28 ANSWER 56 OF 59 CAPLUS COPYRIGHT 2003 ACS
TI DNA gene

L28 ANSWER 57 OF 59 MEDLINE DUPLICATE 27
TI Differential expression of cloned mouse metallothionein sequences in Escherichia coli.

L28 ANSWER 58 OF 59 MEDLINE DUPLICATE 28
TI Secretion of Escherichia coli beta-lactamase from Bacillus subtilis by the aid of alpha-amylase signal sequence.

L28 ANSWER 59 OF 59 MEDLINE DUPLICATE 29
TI Cloning and expression of a Bacillus coagulans amylase gene in Escherichia coli.

=> d 9 bib ab

L28 ANSWER 9 OF 59 MEDLINE DUPLICATE 4
AN 95028148 MEDLINE
DN 95028148 PubMed ID: 7941736
TI Use of beta-lactamase as a secreted reporter of **promoter** function in yeast.
AU Cartwright C P; Li Y; Zhu Y S; Kang Y S; Tipper D J
CS University of Massachusetts Medical School, Department of Molecular Genetics and Microbiology, Worcester 01655.
NC GM-20755 (NIGMS)
SO YEAST, **(1994 Apr)** 10 (4) 497-508.
Journal code: 8607637. ISSN: 0749-503X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199411
ED Entered STN: 19941222
Last Updated on STN: 19941222
Entered Medline: 19941115
AB K1 preprotoxin is the 316 residue precursor of the K1 killer toxin secreted by the yeast Saccharomyces cerevisiae. The SP beta la reporter consists of the mature, secreted form of beta-**lactamase** (beta la) **fused** to S and P, two fragments of preprotoxin. S is the N-terminal 34 residues, including the secretion signal. P, a 67 residue 'processing' segment with three sites for N-glycosylation, terminates in a Lys Arg site for cleavage by the Kex2 protease. Expression of SP beta 1a in yeast results in efficient secretion, processing by signal peptidase and glycosylation in the endoplasmic reticulum, producing pro beta la. Kex2 cleavage of pro beta la in the lumen of a late Golgi compartment releases beta la, which accumulates stably in culture media buffered at pH 5.8-7. The half-life of secretion is 11 min at 30 degrees C; 10-12% of the total activity in exponential-phase cells is intracellular, mostly in the form of pro beta la, indicating that transit from the endoplasmic reticulum to the Golgi is rate limiting. We have used SP beta la expression in single- and multi-copy vectors to compare the PGK, GAL1, GAL10, PHO5 and CUP1 **promoters** under varying nutritional conditions. In exponential-phase cells, secretion of beta la over a 40-fold range and up to several micrograms/ml was proportional to transcript level, demonstrating that SP beta la can be employed as a convenient secreted reporter of **promoter** function in yeast.

=> d 13 bib ab

L28 ANSWER 13 OF 59 CAPLUS COPYRIGHT 2003 ACS
AN 1995:230022 CAPLUS
DN 122:73293
TI Universal .beta.-galactosidase cloning vectors for **promoter** analysis and gene targeting
AU Kaestner, Klaus H.; Montoliu, Luis; Kern, Heidrun; Thulke, Monika;

Schuetz, Guenther
CS Division Molecular Biology of the Cell I, German Cancer Research Center, Heidelberg, D-69120, Germany
SO Gene (**1994**), 148(1), 67-70
CODEN: GENED6; ISSN: 0378-1119
PB Elsevier
DT Journal
LA English
AB Two new plasmid vectors suitable for generating fusions with the lacZ gene were developed and tested. The vectors can be applied in the anal. of regulatory elements of eukaryotic genes in both transient and stable transfection expts. In addn., they can be utilized as the backbone of gene targeting vectors, allowing the assessment of the expression pattern of the targeted gene by staining for .beta.-galactosidase activity.

=> s gene (9a) target?
L29 57559 GENE (9A) TARGET?

=> s l29 and lactam?
L30 125 L29 AND LACTAM?

=> dup rem l30
PROCESSING COMPLETED FOR L30
L31 85 DUP REM L30 (40 DUPLICATES REMOVED)

=> d 50 bib

L31 ANSWER 50 OF 85 MEDLINE
AN 1998417789 MEDLINE
DN 98417789 PubMed ID: 9745268
TI Identification of penicillin-resistant Streptococcus pneumoniae in nasopharynx of patient with acute otitis media by PCR.
AU Hotomi M; Ubukata K; Konno M; Samukawa T; Shimada J; Suzumoto M; Yamanaka N
CS Department of Otorhinolaryngology, Wakayama Medical College.
SO NIPPON JIBIINKOKA GAKKAI KAIHO [JOURNAL OF THE OTO-RHINO-LARYNGOLOGICAL SOCIETY OF JAPAN], (1998 Jul) 101 (7) 924-30.
Journal code: 7505728. ISSN: 0030-6622.
CY Japan
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA Japanese
FS Priority Journals
EM 199812
ED Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981208

=> d 51-85 ti

L31 ANSWER 51 OF 85 MEDLINE DUPLICATE 11
TI Antisense inhibition of **gene** expression in bacteria by PNA **targeted** to mRNA.

L31 ANSWER 52 OF 85 CAPLUS COPYRIGHT 2003 ACS
TI A new theta-type thermosensitive replicon from Lactococcus lactis as an integration vector for Enterococcus faecalis

L31 ANSWER 53 OF 85 CAPLUS COPYRIGHT 2003 ACS
TI Versatile insertion plasmids for targeted genome manipulations in

bacteria: isolation, deletion, and rescue of the pathogenicity island LEE of the Escherichia coli O157:H7 genome

L31 ANSWER 54 OF 85 MEDLINE DUPLICATE 12
TI Pentapeptide scanning mutagenesis: random insertion of a variable five amino acid cassette in a target protein.

L31 ANSWER 55 OF 85 MEDLINE DUPLICATE 13
TI Identification of a penicillin-binding protein 3 homolog, PBP3x, in Pseudomonas aeruginosa: gene cloning and growth phase-dependent expression.

L31 ANSWER 56 OF 85 MEDLINE
TI Mechanisms of endogenous drug resistance acquisition by spontaneous chromosomal gene mutation.

L31 ANSWER 57 OF 85 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI Construction of transgenic mice carrying a lacI **target gene** with reduced CpG content.

L31 ANSWER 58 OF 85 CAPLUS COPYRIGHT 2003 ACS
TI Isolation of the Pichia pastoris glyceraldehyde-3-phosphate dehydrogenase gene and regulation and use of its promoter

L31 ANSWER 59 OF 85 CAPLUS COPYRIGHT 2003 ACS
TI Rapid construction in yeast of complex **targeting** vectors for **gene** manipulation in the mouse

L31 ANSWER 60 OF 85 CAPLUS COPYRIGHT 2003 ACS
TI The import receptor for the peroxisomal targeting signal 2 (PTS2) in Saccharomyces cerevisiae is encoded by the PAS7 gene

L31 ANSWER 61 OF 85 MEDLINE DUPLICATE 14
TI Effect of amplification or **targeted** disruption of the beta-**lactamase gene** of Nocardia **lactamdurans** on cephamycin biosynthesis.

L31 ANSWER 62 OF 85 CAPLUS COPYRIGHT 2003 ACS
TI Shuffling mutagenesis using pools of randomly-fragmented target DNA, PCR reassembly and in vitro and in vivo recombination in the creation of large libraries

L31 ANSWER 63 OF 85 MEDLINE
TI Analysis of Vibrio cholerae ToxR function by construction of novel fusion proteins.

L31 ANSWER 64 OF 85 MEDLINE DUPLICATE 15
TI The extreme C-terminus is required for secretion of both the native polygalacturonase (PehA) and PehA-Bla hybrid proteins in Erwinia carotovora subsp. carotovora.

L31 ANSWER 65 OF 85 CAPLUS COPYRIGHT 2003 ACS
TI The Hansenula polymorpha PER1 gene is essential for peroxisome biogenesis and encodes a peroxisomal matrix protein with both carboxy- and amino-terminal targeting signals

L31 ANSWER 66 OF 85 CAPLUS COPYRIGHT 2003 ACS
TI Beta-**lactamase** topology probe analysis of the OutO NMePhe peptidase, and six other Out protein components of the Erwinia carotovora general secretion pathway apparatus

L31 ANSWER 67 OF 85 CAPLUS COPYRIGHT 2003 ACS

TI Universal .beta.-galactosidase cloning vectors for promoter analysis and **gene targeting**

L31 ANSWER 68 OF 85 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI Analysis of the regulation of penicillin biosynthesis in Aspergillus nidulans by **targeted** disruption of the acvA **gene**.

L31 ANSWER 69 OF 85 MEDLINE DUPLICATE 16
TI Precursor flux control through **targeted** chromosomal insertion of the lysine epsilon-aminotransferase (lat) **gene** in cephamycin C biosynthesis.

L31 ANSWER 70 OF 85 MEDLINE DUPLICATE 17
TI Critical amino acids responsible for converting specificities of proteins and for enhancing enzyme evolution are located around beta-turn potentials: data-based prediction.

L31 ANSWER 71 OF 85 MEDLINE DUPLICATE 18
TI Effects of plasmid copy number and runaway plasmid replication on overproduction and excretion of beta-**lactamase** from Escherichia coli.

L31 ANSWER 72 OF 85 MEDLINE
TI Rapid detection of mecA gene by nested PCR for diagnosis of methicillin resistance in Staphylococcus aureus.

L31 ANSWER 73 OF 85 CAPLUS COPYRIGHT 2003 ACS
TI Integration of peptides into membranes using a sequence from immunoglobulin M

L31 ANSWER 74 OF 85 CAPLUS COPYRIGHT 2003 ACS
TI Modulation of the production of secondary metabolites

L31 ANSWER 75 OF 85 MEDLINE DUPLICATE 19
TI The anti-gene strategy: control of gene expression by triplex-forming-oligonucleotides.

L31 ANSWER 76 OF 85 CAPLUS COPYRIGHT 2003 ACS
TI Extracting information from protein sequences using random replacement mutagenesis

L31 ANSWER 77 OF 85 MEDLINE DUPLICATE 20
TI Gene disruption of the pcbAB gene encoding ACV synthetase in Cephalosporium acremonium.

L31 ANSWER 78 OF 85 CAPLUS COPYRIGHT 2003 ACS
TI Lymphocyte homing receptors

L31 ANSWER 79 OF 85 CAPLUS COPYRIGHT 2003 ACS
TI Selective inhibition of gene expression by photoactivatable oligonucleotides

L31 ANSWER 80 OF 85 MEDLINE DUPLICATE 21
TI On the evolution of Tn21-like multiresistance transposons: sequence analysis of the gene (aacC1) for gentamicin acetyltransferase-3-I(AAC(3)-I), another member of the Tn21-based expression cassette.

L31 ANSWER 81 OF 85 MEDLINE DUPLICATE 22
TI Precise insertion of antibiotic resistance determinants into Tn21-like transposons: nucleotide sequence of the OXA-1 beta-**lactamase** gene.

L31 ANSWER 82 OF 85 MEDLINE DUPLICATE 23
TI Targeting of a chimeric human histone fusion mRNA to membrane-bound polysomes in HeLa cells.

L31 ANSWER 83 OF 85 MEDLINE DUPLICATE 24
TI Repressor gene, blaI, for Bacillus licheniformis 749 beta-**lactamase**.

L31 ANSWER 84 OF 85 MEDLINE DUPLICATE 25
TI Evolution of an inducible penicillin-**target** protein in methicillin-resistant Staphylococcus aureus by **gene** fusion.

L31 ANSWER 85 OF 85 CAPLUS COPYRIGHT 2003 ACS
TI Targeted point mutation that creates a unique EcoRI site within the signal codons of the .beta.-**lactamase** gene without altering enzyme secretion or processing

=> d 51, 54 59 bib ab

L31 ANSWER 51 OF 85 MEDLINE DUPLICATE 11
AN 1998216567 MEDLINE
DN 98216567 PubMed ID: 9555726
TI Antisense inhibition of **gene** expression in bacteria by PNA **targeted** to mRNA.
AU Good L; Nielsen P E
CS Department of Biochemistry B, Panum Institute, University of Copenhagen, Denmark.
SO NATURE BIOTECHNOLOGY, (1998 Apr) 16 (4) 355-8.
Journal code: 9604648. ISSN: 1087-0156.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199805
ED Entered STN: 19980611
Last Updated on STN: 19980611
Entered Medline: 19980529
AB Peptide nucleic acid (PNA) is a DNA mimic with attractive properties for developing improved **gene-targeted** antisense agents. To test this potential of PNA in bacteria, PNAs were designed to target the start codon regions of the Escherichia coli beta-galactosidase and beta-**lactamase** genes. Dose-dependent and specific gene inhibition was observed in vitro using low nanomolar PNA concentrations and in vivo using low micromolar concentrations. Inhibition was more efficient for a permeable E. coli strain relative to wild-type K-12. The potency of the anti-beta-**lactamase** PNAs was abolished by a six base substitution, and inhibition could be re-established using a PNA with compensating base changes. Antisense inhibition of the beta-**lactamase** gene was sufficient to sensitize resistant cells to the antibiotic ampicillin. The results demonstrate gene- and sequence-specific antisense inhibition in E. coli and open possibilities for antisense antibacterial drugs and gene function analyses in bacteria.

L31 ANSWER 54 OF 85 MEDLINE DUPLICATE 12
AN 97263817 MEDLINE
DN 97263817 PubMed ID: 9108174
TI Pentapeptide scanning mutagenesis: random insertion of a variable five amino acid cassette in a target protein.
AU Hallet B; Sherratt D J; Hayes F
CS Microbiology Unit, Department of Biochemistry, University of Oxford, South Parks Road, Oxford OX1 3QU, UK.

SO NUCLEIC ACIDS RESEARCH, (1997 May 1) 25 (9) 1866-7.
Journal code: 0411011. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
ED Entered STN: 19970609
Last Updated on STN: 19990129
Entered Medline: 19970529
AB A new insertion method for probing protein functional organization was developed. The method relies on the random insertion of transposon Tn 4430 and subsequent in vitro deletion of the bulk of the transposon after which a 15 bp insertion remains within the **target gene**. This results in pentapeptide insertions randomly distributed in the **target** protein. Characterization of 23 pentapeptide insertions in TEM-1beta-**lactamase** demonstrated the utility of the method. The phenotypes associated with the mutated beta-**lactamase** proteins equated both with the sorts of local peptide structures in which the pentapeptide insertions occurred and their position in the three-dimensional structure of the enzyme.

L31 ANSWER 59 OF 85 CAPLUS COPYRIGHT 2003 ACS
AN 1996:730175 CAPLUS
DN 126:70874
TI Rapid construction in yeast of complex **targeting** vectors for **gene** manipulation in the mouse
AU Storck, Thorsten; Krueth, Ulrich; Kolhekar, Rohini; Spregnel, Rolf; Seeburg, Peter H.
CS Center Mol. Biology, Univ. Heidelberg, Heidelberg, 69120, Germany
SO Nucleic Acids Research (1996), 24(22), 4594-4595
CODEN: NARHAD; ISSN: 0305-1048
PB Oxford University Press
DT Journal
LA English
AB Targeting vectors for embryonic stem (ES) cells typically contain a mouse gene segment of >7 kb with the neo **gene** inserted for pos. selection of the **targeting** event. More complex targeting vectors carry addnl. genetic elements (e.g lacZ, loxP, point mutations). Here we use homologous recombination in yeast to construct targeting vectors for the incorporation of genetic elements (GEs) into mouse genes. The precise insertion of GEs into any position of a mouse gene segment cloned in an Escherichia coli/yeast shuttle vector is directed by short recombinogenic arms (RAs) flanking the GEs. In this way, complex targeting vectors can be engineered with considerable ease and speed, obviating extensive gene mapping in search for suitable restriction sites.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	43.91	165.18

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CA SUBSCRIBER PRICE	-1.30	-9.76

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 7, 2003 (20030207/UP).

=> file medline biosis caplus esbiobase cancerlit

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.24	165.42

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-9.76

FILE 'MEDLINE' ENTERED AT 08:39:20 ON 14 FEB 2003

FILE 'BIOSIS' ENTERED AT 08:39:20 ON 14 FEB 2003
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FILE 'CANCERLIT' ENTERED AT 08:39:20 ON 14 FEB 2003

=> s (promoter# or gene#) (11a) (trap?)
L32 3968 (PROMOTER# OR GENE#) (11A) (TRAP?)

=>

=> s l32 and (lactam?)
L33 11 L32 AND (LACTAM?)

=> dup rem l33
PROCESSING COMPLETED FOR L33
L34 6 DUP REM L33 (5 DUPLICATES REMOVED)

=> d 1-6 bib ab

L34 ANSWER 1 OF 6 MEDLINE DUPLICATE 1
AN 2002172347 MEDLINE
DN 21902011 PubMed ID: 11891320
TI Design of an HIV-1 lentiviral-based **gene-trap** vector to detect developmentally regulated **genes** in mammalian cells.
AU Lai Zhennan; Han Ina; Park Misun; Brady Roscoe O
CS Developmental and Metabolic Neurology Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD 20892, USA.. laiz@ninds.nih.gov
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2002 Mar 19) 99 (6) 3651-6.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200204
ED Entered STN: 20020321
Last Updated on STN: 20030105
Entered Medline: 20020424
AB The recent development of HIV-1 lentiviral vectors is especially useful

for gene transfer because they achieve efficient integration into nondividing cell genomes and successful long-term expression of the transgene. These attributes make the vector useful for gene delivery, mutagenesis, and other applications in mammalian systems. Here we describe two HIV-1-based lentiviral vector derivatives, pZR-1 and pZR-2, that can be used in **gene-trap** experiments in mammalian cells in vitro and in vivo. Each lentiviral **gene-trap** vector contains a reporter **gene**, either beta-**lactamase** or enhanced green fluorescent protein (EGFP), that is inserted into the U3 region of the 3' long terminal repeat. Both of the trap vectors readily integrate into the host genome by using a convenient infection technique. Appropriate insertion of the vector into genes causes EGFP or beta-**lactamase** expression. This technique should facilitate the rapid enrichment and cloning of the trapped cells and provides an opportunity to select subpopulations of **trapped** cells based on the subcellular localization of reporter **genes**. Our findings suggest that the reporter gene is driven by an upstream, cell-specific promoter during cell culture and cell differentiation, which further supports the usefulness of lentivirus-based **gene-trap** vectors. Lentiviral **gene-trap** vectors appear to offer a wealth of possibilities for the study of cell differentiation and lineage commitment, as well as for the discovery of new genes.

L34 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 2001:851433 CAPLUS
DN 136:1569
TI Interaction trap assays using selectable markers to screen large libraries for protein-protein and protein-nucleic acid interactions
IN Joung, J. Keith; Miller, Jeffrey; Pabo, Carl O.
PA Massachusetts Institute of Technology, USA
SO PCT Int. Appl., 196 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001088197	A2	20011122	WO 2001-US15718	20010516

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-204509P P 20000516
AB The present invention provides methods and compns. for interaction trap assays for detecting protein-protein, protein-DNA, or protein-RNA interactions using prokaryotic or microbial eukaryotic hosts. The methods and compns. of the invention may also be used to identify agents which may agonize or antagonize a protein-protein, protein-DNA, or protein-RNA interaction. In certain embodiments, the interaction trap system of the invention is useful for screening libraries with greater than 107 members. In other embodiments, the interaction trap system of the invention is used in conjunction with flow cytometry. The invention further provides a means for simultaneously screening a target protein or nucleic acid sequence for the ability to interact with two or more test proteins or nucleic acids. In one form, the screening involves the use of a selectable marker allowing screening of large nos. of cells without the need to scan for a colorimetric marker. In a second form, screening of a

colorimetric marker is by flow cytometry. Screening of a library of 108 members in Escherichia coli for C2H2 zinc finger variants is demonstrated.

L34 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 2001:763177 CAPLUS
DN 135:314424
TI Signal sequence **trapping** from existing **gene** library using a transposon containing a **promoter**-less and signal-less secretion reporter
IN Duffner, Fiona; Wilting, Reinhard; Schnorr, Kirk
PA Novozymes A/S, Den.
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001077315	A1	20011018	WO 2001-DK195	20010322
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1276857	A1	20030122	EP 2001-916937	20010322
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2002076706	A1	20020620	US 2001-823825	20010330
PRAI	DK 2000-576	A	20000407		
	DK 2000-1693	A	20001113		
	DK 2001-210	A	20010209		
	US 2000-198264P	P	20000417		
	US 2000-249237P	P	20001116		
	US 2001-269168P	P	20010215		
	WO 2001-DK195	W	20010322		

AB A method for isolating genes encoding secreted polypeptides from previously established gene-banks or libraries is described in which the endogenous secretion signal sequences are detected using an in vitro transposition reaction where the transposon contains a secretion reporter. The present invention allows the screening for genes encoding secreted, partially secreted, or cell surface-displayed polypeptides of industrial interest, such as enzymes, receptors, cytokines, peptide hormones etc. that would not likely have been isolated using conventional screening assays. The combination of the use of a promoter-less and secretion signal-less secretion reporter gene and an in vitro polynucleotide insertion reaction for the identification of genes encoding secreted, partially secreted, or cell surface displayed polypeptides from genomic or cDNA libraries previously established is described, e.g. the use of a signal-less .beta.-**lactamase** gene comprised in a transposon such as the MuA mini-transposon. Use of the constructed transposon SigA2 contg. a signal-less .beta.-**lactamase gene** in the signal **trapping** of the extracellular pullulanase PULL1012 and xyloglucanase XYG1006 was demonstrated. Use of a transposon which carries the colE1 origin of replication to identify genes coding for secreted proteins in the genome of a host cell was also demonstrated.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 2001:23939 CAPLUS
DN 134:248486
TI Topological analysis of DctQ, the small integral membrane protein of the C4-dicarboxylate TRAP transporter of Rhodobacter capsulatus
AU Wyborn, N. R.; Alderson, J.; Andrews, S. C.; Kelly, D. J.
CS Department of Molecular Biology and Biotechnology, University of Sheffield, Firth Court, Western Bank, Sheffield, S10 2TN, UK
SO FEMS Microbiology Letters (2001), 194(1), 13-17
CODEN: FMLED7; ISSN: 0378-1097
PB Elsevier Science B.V.
DT Journal
LA English
AB Tripartite ATP-independent periplasmic ('TRAP') transporters are a novel group of bacterial and archaeal secondary solute uptake systems, which possess a periplasmic binding protein, but which are unrelated to ATP-binding cassette (ABC) systems. In addn. to the binding protein, TRAP transporters contain two integral membrane proteins or domains, one of which is 40-50 kDa with 12 predicted transmembrane (TM) helixes, thought to be the solute import protein, while the other is 20-30 kDa and of unknown function. Using a series of plasmid-encoded .beta.-**lactamase** fusions, we have detd. the topol. of DctQ, the smaller integral membrane protein from the high-affinity C4-dicarboxylate transporter of Rhodobacter capsulatus, which to date is the most extensively characterized TRAP transporter. DctQ was predicted by several topol. prediction programs to have four TM helixes with the N- and C-termini located in the cytoplasm. The levels of ampicillin resistance conferred by the fusions when expressed in Escherichia coli were found to correlate with this predicted topol. The data have provided a topol. model which can be used to test hypotheses concerning the function of the different regions of DctQ and which can be applied to other members of the DctQ family.
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 5 OF 6 MEDLINE DUPLICATE 2
AN 2000162821 MEDLINE
DN 20162821 PubMed ID: 10697713
TI Developing targets for drug discovery using genome-wide **gene trapping** and ultra-sensitive beta-**lactamase** reporters.
AU Liyanage M; Zamiara E M; Mandurrago B; Riley M; Sanders P; Welchlin H L; Xanthopoulos K G
CS Aurora Biosciences Corporation, San Diego, CA 92121, USA.
SO PROCEEDINGS OF THE WESTERN PHARMACOLOGY SOCIETY, (1999) 42 123-6.
Journal code: 7505899. ISSN: 0083-8969.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200004
ED Entered STN: 20000421
Last Updated on STN: 20000421
Entered Medline: 20000412

L34 ANSWER 6 OF 6 Elsevier BIOBASE COPYRIGHT 2003 Elsevier Science B.V.
AN 1998276858 ESBIOBASE
TI A genome-wide functional assay of signal transduction in living mammalian cells
AU Whitney M.; Rockenstein E.; Cantin G.; Knapp T.; Zlokarnik G.; Sanders P.; Durick K.; Craig F.F.; Negulescu P.A.
CS P.A. Negulescu, Aurora Biosciences Corporation, 11010 Torreyana Rd., San Diego, CA 92121, United States.

E-mail: info@aurorabio.com
SO Nature Biotechnology, (1998), 16/13 (1329-1333), 28 reference(s)
CODEN: NABIF0 ISSN: 1087-0156
DT Journal; Article
CY United States
LA English
SL English
AB We describe a genome-wide functional assay for rapid isolation of cell clones and genetic elements responsive to specific stimuli. A promoterless .beta.-**lactamase** reporter gene was transfected into a human T-cell line to generate a living library of reporter-tagged clones. When loaded with a cell- permeable fluorogenic substrate, the cell library simultaneously reports the expression of a large number of endogenous genes. Flow cytometry was used to recover individual clones whose reporter-tagged genes were either induced or repressed following T-cell activation. Responsive clones were expanded and analyzed pharmacologically to identify patterns of regulation associated with specific genes. Although demonstrated using T cells, the genomic assay could be applied to map downstream transcriptional consequences for any propagating cell line in response to any stimulus of interest.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	19.35	184.77

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.95	-11.71

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 7, 2003 (20030207/UP).

=> s promoterless or promoter(w)less
0 PROMOTERLESS
0 PROMOTER
0 LESS
0 PROMOTER(W)LESS
L35 0 PROMOTERLESS OR PROMOTER(W)LESS

=> file medline biosis caplus cancerlit esbiobase

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.06	184.83

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-11.71

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FILE 'BIOSIS' ENTERED AT 08:41:18 ON 14 FEB 2003
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FILE 'ESBIOBASE' ENTERED AT 08:41:18 ON 14 FEB 2003

=> s promoterless or promoter(w)less
L36 3439 PROMOTERLESS OR PROMOTER(W) LESS

=> \

\ IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l36 and lactam?
L37 57 L36 AND LACTAM?

=> dup rem l37
PROCESSING COMPLETED FOR L37
L38 22 DUP REM L37 (35 DUPLICATES REMOVED)

=> d 1-22 ti

L38 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2003 ACS
TI Signal sequence trapping from existing gene library using a transposon containing a **promoter-less** and signal-less secretion reporter

L38 ANSWER 2 OF 22 MEDLINE
TI Mutations in each of the tol genes of Pseudomonas putida reveal that they are critical for maintenance of outer membrane stability.

L38 ANSWER 3 OF 22 MEDLINE DUPLICATE 1
TI Overexpression of the lat gene in Nocardia **lactamdurans** from strong heterologous promoters results in very high levels of lysine-6-aminotransferase and up to two-fold increase in cephamycin C production.

L38 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2003 ACS
TI pBBR1-GFP: a broad-host-range vector for prokaryotic promoter studies

L38 ANSWER 5 OF 22 MEDLINE DUPLICATE 2
TI A genome-wide functional assay of signal transduction in living mammalian cells.

L38 ANSWER 6 OF 22 MEDLINE DUPLICATE 3
TI Amy as a reporter gene for promoter activity in Nocardia **lactamdurans**: comparison of promoters of the cephamycin cluster.

L38 ANSWER 7 OF 22 MEDLINE DUPLICATE 4
TI Plasmids for heterologous expression in Pasteurella haemolytica.

L38 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2003 ACS
TI Vector for IS element entrapment and functional characterization based on turning on expression of distal **promoterless** genes

L38 ANSWER 9 OF 22 MEDLINE DUPLICATE 5
TI Integrative vectors for constructing single-copy transcriptional fusions

between Bacillus subtilis promoters and various reporter genes encoding heat-stable enzymes.

L38 ANSWER 10 OF 22 MEDLINE DUPLICATE 6
TI Development of a gene reporter system in moderately halophilic bacteria by employing the ice nucleation gene of Pseudomonas syringae.

L38 ANSWER 11 OF 22 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 7
TI The ice nucleation gene from Pseudomonas syringae as a sensitive gene reporter for promoter analysis in Zymomonas mobilis.

L38 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2003 ACS
TI Integrative vectors for constructing single-copy transcriptional fusions between Bacillus subtilis promoters and various reporter genes encoding heat-stable enzymes

L38 ANSWER 13 OF 22 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 8
TI Efficient transformation of the cephamycin C producer Nocardia **lactamdurans** and development of shuttle and promoter-probe cloning vectors.

L38 ANSWER 14 OF 22 MEDLINE DUPLICATE 9
TI Construction of secretion vectors using signal sequence of Bacillus subtilis alkaline protease E gene.

L38 ANSWER 15 OF 22 MEDLINE DUPLICATE 10
TI A series of integrative plasmids for Bacillus subtilis containing unique cloning sites in all three open reading frames for translational lacZ fusions.

L38 ANSWER 16 OF 22 MEDLINE DUPLICATE 11
TI An efficient expression and secretion system based on Bacillus subtilis phage phi 105 and its use for the production of B. cereus beta-**lactamase** I.

L38 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2003 ACS
TI Identification of novel promoters in Lactococcus lactis with promoter probe vectors functional in Gram-positive and Gram-negative bacteria

L38 ANSWER 18 OF 22 MEDLINE DUPLICATE 12
TI Cloning and expression of the ponB gene, encoding penicillin-binding protein 1B of Escherichia coli, in heterologous systems.

L38 ANSWER 19 OF 22 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 13
TI ISOLATION AND CHARACTERIZATION OF ZYMOMONAS-MOBILIS DNA FRAGMENTS SHOWING PROMOTER ACTIVITY IN ESCHERICHIA-COLI.

L38 ANSWER 20 OF 22 MEDLINE DUPLICATE 14
TI Novel rearrangements of IS30 carrying plasmids leading to the reactivation of gene expression.

L38 ANSWER 21 OF 22 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI EFFICIENT INTEGRATIVE TRANSFORMATION OF CEPHALOSPORIUM-ACREMONIUM.

L38 ANSWER 22 OF 22 MEDLINE
TI Cloning and expression of Clostridium pasteurianum galactokinase gene in Escherichia coli K-12 and nucleotide sequence analysis of a region affecting the amount of the enzyme.

=> d 5, 8 bib ab

L38 ANSWER 5 OF 22 MEDLINE DUPLICATE 2
AN 1999068502 MEDLINE
DN 99068502 PubMed ID: 9853613
TI A genome-wide functional assay of signal transduction in living mammalian cells.
CM Comment in: Nat Biotechnol. 1998 Dec;16(13):1311-2
AU Whitney M; Rockenstein E; Cantin G; Knapp T; Zlokarnik G; Sanders P; Durick K; Craig F F; Negulescu P A
CS Aurora Biosciences Corporation, San Diego, CA 92121, USA.
SO NATURE BIOTECHNOLOGY, (1998 Dec) 16 (13) 1329-33.
Journal code: 9604648. ISSN: 1087-0156.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990316
Last Updated on STN: 19990316
Entered Medline: 19990226
AB We describe a genome-wide functional assay for rapid isolation of cell clones and genetic elements responsive to specific stimuli. A **promoterless** beta-**lactamase** reporter gene was transfected into a human T-cell line to generate a living library of reporter-tagged clones. When loaded with a cell-permeable fluorogenic substrate, the cell library simultaneously reports the expression of a large number of endogenous genes. Flow cytometry was used to recover individual clones whose reporter-tagged genes were either induced or repressed following T-cell activation. Responsive clones were expanded and analyzed pharmacologically to identify patterns of regulation associated with specific genes. Although demonstrated using T cells, the genomic assay could be applied to map downstream transcriptional consequences for any propagating cell line in response to any stimulus of interest.

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TI Vector for IS element entrapment and functional characterization based on turning on expression of distal **promoterless** genes
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SO Gene (1996), 174(1), 103-110
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LA English
AB We constructed and characterized a novel trap vector for rapid isolation of insertion sequences. The strategy used for the isolation of IS (insertion sequence) elements is based on the ability of many IS elements to turn on the expression of otherwise silent genes distal to some sites of insertion. The simple transposition of an IS element can sometimes cause the constitutive expression of **promoterless** antibiotic resistance genes resulting in selectable phenotypes. The trap vector pAW1326 is based on a pBR322 replicon, it carries ampicillin and streptomycin resistance genes, and also silenced genes that confer chloramphenicol and kanamycin resistance once activated. The trap vector pAW1326 proved to be efficient and 85 percent of all isolated mutations were insertions. The majority of IS elements resident in the studied Escherichia coli strains tested became trapped, namely IS2, IS3, IS5,

IS150, IS186 and Tn1000. We also encountered an insertion sequence, called IS10L/R-2, which is a hybrid of the two IS variants IS10L and IS10R. IS10L/R-2 is absent from most E. coli strains, but it is detectable in some strains such as JM109 which had been submitted to Tn10 mutagenesis. The distribution of the insertion sequences within the trap region was not random. Rather, the integration of chromosomal mobile genetic elements into the offered target sequence occurred in element-specific clusters. This is explained both by the target specificity and by the specific requirements for the activation of gene transcription by the DNA rearrangement. The employed trap vector pAW1326 proved to be useful for the isolation of mobile genetic elements, for a demonstration of their transposition activity as well as for the further characterization of some of the functional parameters of transposition.